

## THE TICK FEVER PARASITE.

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Tick fever is a disease which appears to be widely distributed throughout the warmer countries of the world. It is primarily an acute anemia, associated with a haematozoon, which feeds upon and destroys the red blood corpuscles. In consequence of the degradation and disintegration of the corpuscles, the capillaries become clogged, the internal organs intensely swollen, and the liver and kidneys being frequently unable to cope with the task of eliminating the products of the corpuscle disintegration, death results from what is essentially capillary congestion. During the very rapid destruction of the corpuscles, the urine may be of a dark red colour and albuminous.

So far as is definitely known, the disease occurs only among cattle, but two diseases of sheep have been described which appear to be caused by the same parasite. In the southern portions of the United States of America it is known as Texas or southern cattle fever; in Italy, East Africa and Turkey as cattle malaria; in the lower reaches of the Danube as haemoglobinuria, and in Sardinia and Finland as haematuria.

Theobald Smith, in conjunction with Kilborne, was the first to give a complete account of the disease and to trace its cause to a haematozoon which he called *Pyrosoma bigeminum*, a name which has been altered by Wasielewski (8) to *Aplosoma bigeminum*, Smith. One year previous to the first of Theobald Smith's papers, Babes had described under the name of haemoglobinuria a disease of cattle in the swampy pastures of the lower Danube in Roumania, and had traced the cause to a haematozoon, but although the disease is now considered to be identical with Texas fever, Babes' description of the parasite was far from being as complete as that of Theobald Smith.

There are two varieties of the disease, the acute and the chronic form. In the former, the destruction of the red corpuscles is very rapid, while in the latter it is much slower. The acute form is marked by the general symptom of rapid oxidation, viz., acute fever, and in the organs of affected animals all known forms of the parasite can be found. In the chronic disease only the supposed younger forms are to be seen. The presence of the parasite in an animal does not necessarily indicate the presence of disease, since it appears to exist latent, (5, 6) becoming evident when the system is weakened from some other disease. Just as the cause of rheumatism, influenza, or even the common cold may presumably remain latent in man to become evident when the system is temporarily weakened as by a sudden chill.

Cattle are the most susceptible of all animals, and although it may be said that tick fever is a bovine disease, it should not be forgotten that other animals succumb to the action of parasites which may be identical with *Apiosoma bigeminum*. There is a canine disease of Lombardy and a sheep disease, carceag or parasitic ictero-haematuria, in both of which the organisms characteristic of tick fever have been observed. Furthermore, according to some authors, rabbits and guinea-pigs succumb when inoculated with blood containing the parasite.

Infection occurs by means of the cattle tick (*Ixodes horis*) in cases of Texas fever, tick fever and haemoglobinuria. In the bovine malaria of the Roman Compagna (3) and of Turkey (6) there is no record of ticks associated with the disease.

The parasite is found in the blood serum and within the red corpuscles. When invaded by the parasite the corpuscle loses its elasticity and is retained in the capillaries and the body organs. Consequently comparatively few invaded corpuscles are to be found in the circulating blood, the percentage varying from 1 to 2 except during the height of the fever, when it may rise to from 5 to 10 in a few cases. The blood of the organs, as for example the heart-substance, has about 80 per cent. of the corpuscles invaded.

The typical form of the parasite is pear-shaped, and although a single organism may occupy the corpuscle, yet commonly they

occur in twos, sometimes even in fives and sixes. When double, the narrow ends are together, and it is undoubtedly only a matter of technique to show that they are united by a connecting thread. The pear-shaped parasite stains unequally; the part occupying the bulb of the pear stains feebly or not at all, and it is assumed that this is a vacuole; the middle portion generally takes the stain deeply. This form is not common in the corpuscle during life, (1) for by the time that the parasite has grown to this shape the corpuscle has become disintegrated and the organism free. It is to be found in numbers soon after death, while if a section or film be made immediately the animal dies, there is seen a mixture of the younger with the presumably oldest form. In the capillaries during the acute stage small double spindles are sometimes seen, each spindle being connected by a joining line. This is probably an intermediate stage of the parasite.

In fresh blood a small round spot is frequently seen close to the periphery in some of the corpuscles; it is free from haemoglobin and measures  $0.5\ \mu$  in diameter. It is also visible in stained preparations, where it varies up to  $0.6\ \mu$ , and is often divided. Since this appears at the beginning of the attack and disappears when the corpuscles begin to increase in number, it is not to be considered as a degenerate form (1). It is contended by Celli and Santori that this extremely small body is not the parasite, since Marciafava had seen it in cases of malaria, and they themselves had found it in healthy guinea-pigs as well as in rabbits and dogs which had died of diseases other than tick fever. It is referred to as a pseudoparasitic endoglobular body. It is possible that the smallest form of the tick fever parasite may be of the same diameter as the pseudoparasitic body; in this case they would be morphologically identical.

According to Celli and Santori, what is really the smallest and probably the youngest type of the parasite measures from 1 to  $1.5\ \mu$ . It changes its shape as it moves about from place to place in the corpuscle, becoming round, oblong, cylindrical, egg- or pear-shaped in succession. It may occur singly, in pairs or threes in one and the same corpuscle. It is strongly refractile and shows

up well against the ground of the corpuscle. Should the mobility cease either naturally or artificially by cooling below  $24^{\circ}$  C. or by killing, the amoeboid parasite becomes round and often shows a central point, which, together with its usual peripheral position, enables it to be recognised. It differs from the pseudoparasitic bodies in being larger, more refractile and motile (3). It occurs in the acute and chronic stages of the disease.

Sidney Hunt and Collins describe a similar multiplicity of form among bodies occurring free in the circulating blood, but especially in the substance of the kidney and the spleen, where they are enormously abundant. They are also found, but to a less extent, in the liver. "These free bodies vary greatly in size, some being no more than  $\frac{1}{20}$  and some as large as  $\frac{1}{3}$  the size of a bovine red blood cell, which is somewhere about  $\frac{1}{4000}$  of an inch," *i.e.*, they vary from 0.8 to 2  $\mu$ . "They vary also in form, the majority being round or spherical, some pear-shaped, some oblong, some sausage-like, others constricted like an hourglass and others irregular. None of these forms are by any means constant, since the bodies are perpetually changing their outline. They differ also in respect to colour; most are colourless and highly refractive, others have a yellowish or even reddish-brown tinge, but there is never any granular pigment. The majority appear homogeneous, others dark-centred, though this latter appearance may be due to their high refraction. A certain proportion are motionless, but the majority are in very active movement, and may sometimes be seen to work their way across the field of the microscope, apparently urged along by a flagellum. The most general and characteristic movement, however, is neither amoeboid nor locomotive, but consists of a peculiar rolling on their own axes, which gives them a twinkling appearance, something like that of a small bright coin as it sinks in deep water." The motility is more active than with the intracorpuseular parasite.

The amoeboid form of the parasite is larger, being from two to three times the size of the smallest motile form of Celli and Santori. The refrangibility is so low that it can only be seen with difficulty in some of its phases, especially when, as is often

the case, the corpuscle is paler than usual. The amoeboid motion is active with the smaller sizes, and slower with the larger. On account of the amoeboid motion, the parasite may appear with one, two, three or more protrusions; it may divide into two, the halves connected by a thread when an appearance is obtained which is probably that described and considered by Theobald Smith as a younger stage of the pear-shape. The two halves join again to form perhaps a diamond or a sphere. The two pear-shaped forms are seldom small; they are generally large, and vary from  $2\cdot5$  to  $4\ \mu$  long, by  $1\cdot5$  to  $2\ \mu$  broad, and have a granule near the swollen end. They may be considered to be in extremely slow amoeboid motion, but so slow as to be practically non-motile or as a particular stage in the developmental cycle. In support of the former hypothesis there is the fact that long observation showed the form to vary from the pear to an egg or round shape; while in another case, also after long observation, an apiosoma without altering its shape disappeared from the corpuscle (3).

In very acute cases of the fever a few large granules have been observed lying separated from one another or in a heap within some of the blood corpuscles. They are non-motile, and retain their rounded shape. Their significance is unknown, but it is suggested that they may be spore forms (3).

Besides the parasitic forms, one frequently observes in the blood, red corpuscles larger than usual, rather pale and beset throughout the different layers with chromatin granules. Since these granules are found in other cases of anaemia as, in the sheep, they have no relation with the parasite, and are to be traced to the caryolysis of the young red corpuscles.

The complete life cycle of the parasite has not yet been described by any author. Theobald Smith suggests that the small motile globule is the youngest intraglobular stage, the globule dividing, each part becoming spindle-shaped and ultimately pear-shaped, the portions being still connected by a thread. In the chronic cases of the fever there is a certain immunity produced, and the later stages of the parasite are suppressed (1). The large pear-shaped body either within or without the corpuscle may begin

a reproductive stage, and produce a generation of very minute bodies akin to the smallest observed stage, or there may be a free reproductive phase in the blood distinct from the intraglobular. These phases have not been seen.

Sidney Hunt (5) notes that in coverglass preparations of advanced cases, the parasites exhibit all the stages between being intra- and extracorpuseular, the corpuscles being more or less dis-integrated. Some of the apiosoma are seen to have a clear central portion which does not stain. The pear-shaped forms are of various sizes, the clear portions being more marked in the larger ones. Sometimes in the blood there are also seen crescent-shaped bodies which Dr. E. Klein, F.R.S., considered to be the stage succeeding the pear-shape, since they are presumably full of young pyrosoma. These crescent-shaped bodies are really sarcosporidia, common muscle parasites.

Like the yeasts, the protozoa do not lend themselves well as objects of study in the dry and stained condition. Yet by exercising care, especially in the choice of a fixing agent, it is possible to obtain specimens which tell us more of the structure of the parasite than can be learnt from their study in the fresh condition. In a number of films of dried blood\* which the writer examined the various recognised phases in the life history of the parasite were observed. The smaller diplococcus bodies measured  $0.4\mu$ , and the larger  $1\mu$ ; both intra- and extra-corpuseular forms occurred. The mature forms varied in size, the difference being mainly due to the vacuole which seems to increase as growth proceeds much more than the other parts of the apiosoma. The staining is irregular; the neck, the middle and the terminal margin of the pear colour deeply; the vacuole faintly or not at all. In some of the corpuscles two refractile spherical bodies are observable, and careful focussing and adjustment of the light revealed the shrivelled remains of the middle and neck of the apiosoma. The growth in the mature form, the persistence and refrangibility point to the so-called vacuole being really a capsule,

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\* Kindly lent by Dr. Frank Tidswell.

and, if so, all the interbovine cycle may be assumed to have been observed. The diplococcus bodies, the amoeba, the mature apiosoma with its capsule complete one portion of the life history. Since the multiplication of the parasite is so rapid it almost follows that all stages of the interbovine life cycle must have been observed by those who investigated the blood. The interpretation alone is wanting, and this is supplied if, for vacuole, we read capsule. Celli and Santori's observations upon fresh specimens bear out this interpretation. They noted that the mature apiosoma had a granule at the swollen end. This appearance would be caused by the refraction of the capsule. They make no mention of a vacuole, nor do they figure one in their drawings. The granule which they represent by a tiny circle occupies a position which coincides with the centre of the capsule. They mention that they saw the pear-shape alter, after a long time, to an egg or round shape. Such a change would be brought about by the enlargement of the capsule and the shrinkage and degradation of the body of the apiosoma concomitant with the maturation and persistence of the capsule. Another observation showed that the apiosoma, without altering its shape, suddenly disappeared from the corpuscle. This would happen were the capsule to rupture and liberate its contents simultaneously with the collapse of the other portions.

With regard to the susceptibility of other animals, Theobald Smith found that rabbits, guinea-pigs, goats and sheep showed neither a multiplication of the parasite nor symptoms of the disease when inoculated with virulent blood. Similarly, Celli and Santori injected virulent blood into rabbits, guinea-pigs, mice, rats, cats and dogs, but without result. They mention, however, that death sometimes ensued, but the parasite could not be found. The pseudo-parasitic forms were present. These authors may be wrong in considering all the small diplococcus bodies as being pseudo-parasitic. Although the parasitic forms were not found, the injected blood maintained its virulence through a series of three guinea-pigs. Nicolle and Adil Bey found that 1 c.c. of virulent blood caused the death of guinea-pigs. Sidney Hunt and Collins

found the horse unaffected, while sheep developed high fever as the result of intravenous inoculation with virulent blood. The small marginal bodies were found in the blood of one of the sheep which was slaughtered, but there were no characteristic apiosoma. The sheep diseases carceag (Babes) and parasitic ictero-haematuria (Bonome) are caused, if not by the same parasite, by an ally so close that it seems only a modification. Babes does not describe the parasite at all fully, but since he claims that his disease and that of Bonome are identical, it will be sufficient to describe the parasite of the latter (7). The infected blood corpuscles have on their margin or inside round, oval or pear-shaped, strong, light-refracting, colourless bodies, varying in size from 1 to  $3\mu$ ; they frequently show active contracting movements. In the plasma they are seen either singly or in twos or threes. They are easily coloured by aniline stains. Organs of locomotion were never observed. The blood of the organs contained a greater number of invaded corpuscles than were to be found in the circulating blood. In the former places the parasites were chiefly the more mature forms, and in the latter chiefly the younger. In the urine the parasite was found partly free and partly in blood corpuscles.

It is admitted by American and Australian investigators that the cattle tick is the infecting agent. European authors must be aware of the part played by the tick in America, and yet no mention of the insect is made in some of their papers. Babes, however, noted that animals suffering from haemoglobinuria were infested with ticks; and Schneidemühl supplements this, saying that the parasite of this fever exists for some time in the body cavities of the tick as in Texas fever: all ticks do not convey the disease, since susceptible cattle may have ticks without any sign of illness. There are, however, varieties of ticks, some of which apparently never produce Texas fever, while others do. But of the dangerous species of tick only those that carry infection are to be feared, and this infectivity is determined by locality. It is self-evident that in a new locality the disease must have begun either with an animal or with a tick: in the latter case the tick



would infect an animal, and other ticks feeding thereon would convey the infection to other animals. But it is well known that a mature tick never leaves one host to attach itself to another; in fact, it is generally accepted that it is only in the larval stage that ticks adhere to cattle. The mature and infected tick, therefore, falls to the ground, and under some cover lays its eggs, which in time hatch, become the larval forms, and attach themselves to a passing animal with poisonous effect. The question, then, comes to be: in what manner is the parasite conveyed from the mother tick to the larval form? Is it carried internally or externally? Does the parasite, when absorbed by the tick, pass through the alimentary canal to infect the ground; the exterior of the eggs and ultimately the larval tick which inoculates the parasite into the animal after the manner of a solid inoculating needle; or does the parasite enter an alternative phase in its life-history in the body of the tick? One cannot say how the parasite gets from the parent to the larva, but that it certainly does and directly has been proved by the experiments of Theobald Smith and Kilborne, who hatched tick eggs in the laboratory and produced the disease by fastening the larvæ on susceptible animals. Prof. Mayo, of Kansas, also produced a fatal attack by placing upon a cow the larvæ hatched from mature ticks that had been sent by mail from Texas. These experiments, however, do not decide the question as to whether the parasite exists inside or outside the egg capsule. It would be interesting to know if larvæ hatched from disinfected eggs could produce the disease. If they could not, the search for a phase of the parasite in the body of the tick might be useless. Another point worthy of consideration is whether the tick may not mechanically carry the parasite from the pasture into the animal. We frequently hear of such mechanical inoculation by biting insects such as bugs and gnats, and in the case of louping-ill, a sheep disease of Scotland and the North of England, where infection is in all probability carried by the sheep tick, all evidence goes to show that the infection is carried mechanically by the insect. Theobald Smith considers it to be quite possible that biting or stinging and blood-sucking insects may transmit

the parasite directly from susceptible animal to susceptible animal, or perhaps there may be the intermediate stage of a non-susceptible animal. Owing to the long incubation period, he could not, however, obtain data in support of this view. With regard to the possibility of the tick conveying the parasite from the pasture to the animal, it may be well to consider how the pasture may become infected. Infection has been produced artificially by scattering mature ticks from infected animals over the ground, and such seems to be the only method recognised at present whereby infection may occur, viz, by the infected ticks falling off the animal. If the tick acts only or partly as a mechanical agent in carrying the parasite, the infection of the pasture is of paramount importance. Such infection is chiefly caused by animals suffering from the fever. But it is also possible that animals which have recovered, and the blood of which still contains the parasite, as well as animals which, bred in an infected country, have the parasite latent in their system, probably through repeated tick inoculation, may also form the nucleus of an outbreak. Preventive inoculation by the use of what is known as recovered blood—that is, the blood of animals which have recovered from the disease—is a process which may not be unattended with danger. The practice would be innocuous did the recovered blood contain no parasite, but this cannot be said to be the case. As a result of the inoculation, the animal develops the fever, and during this time at least the blood will contain the parasite. One cannot doubt that a single tick sucking this blood may be the means of starting the disease in a new locality. But to return to the infection of the pasture, during an acute attack of the fever the animal is constipated, passing dung which is frequently blood-stained, and since the blood harbours the parasite a transference of the causative agent to the pasture occurs. The kidneys are found charged with the parasite, and since they are in a pathological condition it seems possible that the protozoon may pass into the urine. Although the latter has often been examined, the parasite has never been found in it with certainty.

Bonome (7) found the parasite in the urine of sheep suffering from parasitic ictero-haematuria. Against the view that the tick carries the parasite directly from the ground to the animal, are the experiments performed in America and Queensland, (4) showing that a strained watery emulsion of crushed larval ticks does not produce the disease. If these experiments are to be trusted as indicating a fact, viz., that on or in the larval tick there are no cattle parasites, there only remains the probability that the cattle parasite is matured in the body of the tick from an alternative form which may be called the tick parasite. This view is the one at present held, being engendered by these experiments and also perhaps on account of some similarity between Texas fever and malaria.

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#### LITERATURE.

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